CLAIMS:

1. A method of screening a sample of body fluid for at least one autoantibody to at least one antigen, which method comprises:

(a) providing a source of said at least one antigen to said autoantibody;

(b) providing a substrate having immobilised thereto at least one antibody to said antigen of step (a);

(c) contacting said antigen source of step (a) with said sample of body fluid, so as to obtain a mixture wherein said antigen is allowed to substantially bind with said autoantibody, when the latter is present in said sample;

(d) allowing said mixture obtained in step (c) to flow relative to said substrate of step (b) so as to allow said mixture to contact said antibody immobilised to said substrate;

(e) providing labelling means so as to permit monitoring of binding of said autoantibody and said antigen present in said mixture obtained in step (c); and

(f) monitoring said binding so as to provide an indication of the presence of said autoantibody in said sample of body fluid.

2. A method according to claim 1, wherein said antigen comprises a thyroid protein.

3. A method according to claim 2, wherein said thyroid protein is selected from the group consisting of thyroid peroxidase, thyroglobulin and thyroid stimulating hormone receptor.

4. A method according to claim 3, wherein said thyroid protein is selected from the group consisting of thyroid peroxidase and thyroglobulin.

5. A method of screening a sample of body fluid for at least one autoantibody to at least one antigen comprising a thyroid protein selected from the group consisting of thyroid peroxidase, thyroglobulin and thyroid stimulating hormone receptor, which method comprises:

(a) providing a source of said at least one antigen to said autoantibody;

(b) providing a substrate having immobilised thereto at least one antibody to said antigen of step (a);

(c) contacting said antigen source of step (a) with said sample of body fluid, so as to obtain a mixture wherein said antigen is allowed to substantially bind with said autoantibody, when the latter is present in said sample;

(d) allowing said mixture obtained in step (c) to flow relative to said substrate of step (b) so as to allow said mixture to contact said antibody

immobilised to said substrate;

(e) providing labelling means so as to permit monitoring of binding of said autoantibody and said antigen present in said mixture obtained in step (c); and

(f) monitoring said binding so as to provide an indication of the presence of said autoantibody in said sample of body fluid.

6. A method according to claim 5, wherein said thyroid protein is thyroid peroxidase or thyroglobulin.

7. A method according to any of claims 1 to 6, which further comprises screening for the presence of at least one of thyroid stimulating hormone, thyroxine, tri-iodothyronine and thyroglobulin in said sample of body fluid.

8. A method according to any preceding claim, which comprises contacting in step (c) said antigen source and said sample of body fluid with at least one substantially non-immobilised antibody to said antigen.

9. A method according to claim 8, wherein said non-immobilised antibody is provided in substantially purified form.

10. A method according to claim 8 or 9, wherein said non-immobilised antibody comprises a monoclonal antibody.

11. A method according to any of claims 8 to 10, wherein said non-immobilised antibody comprises an autoantibody to said antigen.

12. A method according to any preceding claim, wherein said monitoring in step (f) comprises observing a colorimetric change dependent on said binding of said autoantibody and said antigen present in said mixture of step (c).

13. A method according to claim 12, wherein said labelling means include colloidal gold.

14. A method according to any preceding claim, which further comprises providing a positive control that is present in the presence or absence of the autoantibody or autoantibodies being screened.

15. A method according to any preceding claim, wherein said mixture obtained in step (c) is allowed to flow along said substrate and interact with said antibody immobilised to said substrate.

16. A method according to claim 15, wherein at least said sample of body fluid is contacted with an application zone of said substrate, which application zone is provided upstream on said substrate relative to said immobilised antibody, and wherein said mixture is allowed to flow from said application zone along said

substrate so as to interact with said immobilised antibody.

17. A method according to claim 16, wherein said application zone includes said source of said antigen of step (a), and said mixture in step (c) is obtained by contacting said sample of body fluid with said antigen of said application zone.

18. A method according to claim 16 or 17 as dependent on any of claims 8 to 11, wherein said application zone further includes said non-immobilised antibody, and said mixture in step (c) is obtained by contacting said sample of body fluid and said antigen with said non-immobilised antibody present in said application zone.

19. A method according to claim 16, wherein said antigen source of step (a) and said sample of body fluid are contacted substantially remote from said substrate so as to provide said mixture of step (c), and said mixture is subsequently contacted with said application zone.

20. A method according to claim 19 as dependent on any of claims 8 to 11, wherein said antigen source of step (a), said sample of body fluid and/or said non-immobilised antibody are contacted substantially remote from said substrate so as to provide said mixture of step (c), and said mixture is subsequently

~~contacted with said application zone.~~

21. A method according to any preceding claim, wherein said substrate comprises a membrane of nitrocellulose, cellulose acetate or a polyamide.

22. A method according to any preceding claim, wherein said immobilised antibody is in substantially purified form.

23. A method according to any preceding claim, wherein said immobilised antibody comprises an autoantibody to said antigen.

24. A method according to any of claims 1 to 23, wherein said immobilised antibody comprises a monoclonal antibody.

25. A method according to any preceding claim, wherein said sample of body fluid comprises blood, plasma, serum or urine.

26. A method according to any preceding claim, which comprises screening said sample of body fluid for one said autoantibody.

27. A method according to claim 26, wherein said antigen includes a binding site to which either said autoantibody or said immobilised antibody can bind, ~~whereby in step (d) binding of said immobilised~~

~~antibody to said binding site is substantially~~ precluded where said autoantibody has substantially bound to said binding site in step (c).

28. A method according to any of claims 1 to 25, which comprises screening said sample of body fluid for at least first and second autoantibodies to said antigen, wherein at least first and second antibodies to said antigen are immobilised on said substrate in step (b).

29. A method according to claim 28, wherein said antigen includes:

a first binding site to which either said first autoantibody or said first immobilised antibody can bind, whereby in step (d) binding of said first immobilised antibody to said first binding site is substantially precluded where said first autoantibody has substantially bound to said first binding site in step (c); and

a second binding site to which either said second autoantibody or said second immobilised antibody can bind, whereby in step (d) binding of said second immobilised antibody to said second binding site is substantially precluded where said second autoantibody has substantially bound to said second binding site in step (c);

~~wherein said first and second binding sites are~~

substantially distinct sites on said antigen.

30. A method according to any of claims 26 to 29, wherein said antigen is provided with said labelling means.

31. A method according to any of claims 26 to 30, as dependent on claim 14, wherein said positive control comprises attaching to the substrate at least one control antibody to the antigen, which control antibody binds to a site on the antigen distinct to a binding site thereof for the autoantibody or autoantibodies being screened.

32. A method according to any of claims 26 to 29 as dependent on any of claims 8 to 11, wherein said non-immobilised antibody is provided with said labelling means, which non-immobilised antibody is capable of binding to a site on said antigen substantially distinct from a binding site for either (i) said autoantibody or autoantibodies being screened or (ii) said immobilised antibody, whereby in step (d), antigen is allowed to be substantially bound both to said immobilised antibody and to said non-immobilised antibody.

33. A method according to any of claims 8 to 25 as dependent on any of claims 8 to 11, which comprises screening said sample of body fluid for at least first and second autoantibodies to said antigen, wherein said non-immobilised antibody is capable of binding to

a site on said antigen to which either said first or second autoantibody can bind and which is substantially distinct to a binding site on said antigen for said immobilised antibody, whereby in step (d) antigen is allowed to be substantially bound both to said immobilised antibody and to said non-immobilised antibody.

34. A method according to claim 33, wherein said antigen includes:

a first binding site to which either said first autoantibody or said immobilised antibody can bind, whereby in step (d) binding of immobilised antibody to said first binding site is substantially precluded, where said first autoantibody has substantially bound to said first binding site in step (c); and

a second binding site to which either said second autoantibody or said non-immobilised antibody can bind;

wherein said first and second binding sites are substantially distinct sites on said antigen.

35. A method according to claim 33 or 34, wherein said non-immobilised antibody is provided with said labelling means.

36. A method according to claims 33 to 35 as dependent on claims 11 and 23, wherein said immobilised antibody comprises a first autoantibody to said antigen and said non-immobilised antibody comprises a second autoantibody to said antigen.

37. A method according to any of claims 32 to 36, wherein the positive control comprises attaching to the substrate at least one control agent that can bind to the at least one substantially non-immobilised antibody.

38. A kit for use in screening a sample of body fluid for at least one autoantibody to at least one antigen, which kit comprises:

(a) a source of said at least one antigen to said autoantibody;

(b) a substrate having immobilised thereto at least one antibody to said antigen;

(c) means for contacting said antigen source with said sample of body fluid, so as to obtain a mixture wherein said antigen is allowed to substantially bind with said autoantibody, when the latter is present in said sample;

(d) means for allowing said mixture to flow relative to said substrate so as to allow said mixture to contact said antibody immobilised to said substrate;

(e) labelling means to permit monitoring of binding

~~of said autoantibody and said antigen present in~~ said mixture; and

(f) means for monitoring said binding so as to provide an indication of the presence of said autoantibody in said sample of body fluid.

39. A kit according to claim 38, wherein said antigen comprises a thyroid protein.

40. A kit according to claim 39, wherein said thyroid protein is selected from the group consisting of thyroid peroxidase, thyroglobulin and thyroid stimulating hormone receptor.

41. A kit according to claim 40, wherein said thyroid protein is selected from the group consisting of thyroid peroxidase and thyroglobulin.

42. A kit for use in screening a sample of body fluid for at least one autoantibody to at least one antigen comprising a thyroid protein selected from the group consisting of thyroid peroxidase, thyroglobulin and thyroid stimulating hormone receptor, which kit comprises:

(a) a source of said at least one antigen to said autoantibody;

(b) a substrate having immobilised thereto at least one antibody to said antigen;

~~(c) means for contacting said antigen source with~~

said sample of body fluid, so as to obtain a mixture wherein said antigen is allowed to substantially bind with said autoantibody, when the latter is present in said sample;

(d) means for allowing said mixture to flow relative to said substrate so as to allow said mixture to contact said antibody immobilised to said substrate;

(e) labelling means to permit monitoring of binding of said autoantibody and said antigen present in said mixture; and

(f) means for monitoring said binding so as to provide an indication of the presence of said autoantibody in said sample of body fluid.

43. A kit according to claim 42, wherein said thyroid protein is thyroid peroxidase or thyroglobulin.

44. A kit according to any of claims 38 to 43, which further comprises means for screening for the presence of at least one of thyroid stimulating hormone, thyroxine, tri-iodothyronine and thyroglobulin in said sample of body fluid.

45. A kit according to any of claims 38 to 44, which further comprises a source of at least one substantially non-immobilised antibody to said antigen and means whereby said non-immobilised antibody can be contacted with said antigen source and said sample of body fluid.

46. A kit according to claim 45, wherein said non-immobilised antibody is provided in substantially purified form.

47. A kit according to claim 45 or 46, wherein said non-immobilised antibody comprises a monoclonal antibody.

48. A kit according to any of claims 45 to 47, wherein said non-immobilised antibody comprises an autoantibody to said antigen.

49. A kit according to any of claims 38 to 48, wherein said monitoring means comprise means for observing a colorimetric change dependent on said binding of said autoantibody and said antigen present in said mixture.

50. A kit according to claim 49, wherein said labelling means include colloidal gold.

51. A kit according to any of claims 38 to 50, which further comprises a positive control that is present in the presence or absence of the autoantibody being screened.

52. A kit according to any of claims 38 to 51, wherein said substrate comprises an application zone for at least said sample of body fluid, which application zone is provided upstream on said substrate relative to said immobilised antibody, whereby said mixture is

allowed to flow from said application zone along said substrate so as to interact with said immobilised antibody.

53. A kit according to claim 52, wherein said application zone includes said source of said antigen, and said mixture is obtained by contacting said sample of body fluid with said antigen of said application zone.

54. A kit according to claim 52 or 53 as dependent on any of claims 45 to 48, wherein said application zone further includes said non-immobilised antibody, and means whereby said mixture is obtained by contacting said sample of body fluid and said antigen with said non-immobilised antibody present in said application zone.

55. A kit according to claim 52, wherein means are provided whereby said antigen source and said sample of body fluid are contacted substantially remote from said substrate so as to provide said mixture and means whereby said mixture is subsequently contacted with said application zone.

56. A kit according to claim 55 as dependent on any of claims 45 to 48, wherein means are provided whereby said antigen source, said sample of body fluid and/or said non-immobilised antibody are contacted substantially remote from said substrate so as to provide said mixture, and means whereby said mixture

is subsequently contacted with said application zone.

57. A kit according to any of claims 38 to 56, wherein said substrate comprises a membrane of nitrocellulose, cellulose acetate or a polyamide.

58. A kit according to any of claims 38 to 57, wherein said immobilised antibody is provided in substantially purified form.

59. A kit according to any of claims 38 to 58, wherein said immobilised antibody comprises an autoantibody to said antigen.

60. A kit according to any of claims 38 to 59, wherein said immobilised antibody comprises a monoclonal antibody.

61. A kit according to any of claims 38 to 60, wherein said sample of body fluid comprises blood, plasma, serum or urine.

62. A kit according to any of claims 38 to 61, for screening said sample of body fluid for one said autoantibody, wherein said antigen includes a binding site to which either said autoantibody or said immobilised antibody can bind, whereby binding of said immobilised antibody to said binding site is substantially precluded where said autoantibody has previously substantially bound to said binding site.

~~63. A kit according to any of claims 38 to 61, for~~ screening said sample of body fluid for at least first and second autoantibodies to said antigen, wherein at least first and second antibodies to said antigen are immobilised on said substrate.

64. A kit according to claim 63, wherein said antigen includes:

a first binding site to which either said first autoantibody or said first immobilised antibody can bind, whereby binding of said first immobilised antibody to said first binding site is substantially precluded where said first autoantibody has previously substantially bound to said first binding site; and

a second binding site to which either said second autoantibody or said second immobilised antibody can bind, whereby binding of said second immobilised antibody to said second binding site is substantially precluded where said second autoantibody has previously substantially bound to said second binding site;

wherein said first and second binding sites are substantially distinct sites on the antigen.

~~65. A kit according to any of claims 61 to 64, wherein~~

~~said antigen is provided with said labelling means.~~

66. A kit according to any of claims 62 to 65, as dependent on claim 51, wherein the positive control comprises attaching to the substrate at least one control antibody to the antigen, which control antibody binds to a site on the antigen distinct to a binding site thereof for the autoantibody or autoantibodies being screened.

67. A kit according to any of claims 62 to 64, as dependent on any of claims 45 to 48, wherein said non-immobilised antibody is provided with said labelling means, which non-immobilised antibody is capable of binding to a site on said antigen substantially distinct from a binding site for either (i) said autoantibody or autoantibodies being screened or (ii) said immobilised antibody, whereby antigen is allowed to be substantially bound both to said immobilised antibody and to said non-immobilised antibody.

68. A kit according to any of claims 38 to 61, as dependent on any of claims 45 to 48 for screening said sample of body fluid for at least first and second autoantibodies to said antigen, wherein said non-immobilised antibody is capable of binding to a site on said antigen to which either said first or second autoantibody can bind and which is substantially distinct to a binding site on said antigen for said ~~immobilised antibody, whereby antigen is allowed to be~~

substantially bound both to said immobilised antibody and to said non-immobilised antibody.

69. A kit according to claim 68, wherein said antigen includes:

a first binding site to which either said first autoantibody or said immobilised antibody can bind, whereby binding of immobilised antibody to said first binding site is substantially precluded where said first autoantibody has previously substantially bound to said first binding site; and

a second binding site to which either said second autoantibody or said non-immobilised antibody can bind;

wherein said first and second binding sites are substantially distinct sites on said antigen.

70. A kit according to claim 68 or 69, wherein said non-immobilised antibody is provided with said labelling means.

71. A kit according to any of claims 68 to 70, as dependent on claims 48 and 59, wherein said immobilised antibody comprises a first autoantibody to said antigen and said non-immobilised antibody comprises a second autoantibody to said antigen.

72. A kit according to any of claims 67 to 71, as dependent on claim 51, wherein the positive control comprises attaching to the substrate at least one control agent that can bind to the at least one substantially non-immobilised antibody.

73. Use of a kit according to any of claims 38 to 72, in screening a sample of body fluid for at least one autoantibody to at least one antigen.

74. A method of screening a patient for at least one autoantibody to at least one antigen, which method comprises:

(a) obtaining a sample of body fluid from said patient;

(b) contacting said sample of body fluid of step (a) with an antigen source of a kit according to any of claims 38 to 72, so as to obtain a mixture wherein said antigen is allowed to substantially bind with said autoantibody, when the latter is present in said sample;

(c) allowing said mixture to flow relative to a substrate of a kit according to any of claims 38 to 72, so as to allow said mixture to contact said antibody immobilised to said substrate; and

(d) monitoring binding of said autoantibody and said antigen present in said mixture, so as to provide an indication of the presence of said

autoantibody in said sample of body fluid from said patient.

75. A method according to claim 74, for testing said patient for an autoimmune thyroid disease.

76. A method according to claim 74 or 75, which further comprises screening for the presence of at least one of thyroid stimulating hormone, thyroxine, tri-iodothyronine and thyroglobulin in said sample of body fluid.

77. A method of treating a patient suffering from, or susceptible to, an autoimmune disease, which method comprises:

screening said patient for at least one autoantibody to at least one antigen as defined in any of claims 74 to 76; and

when at least one autoantibody is detected in a sample of body fluid obtained from said patient at a level indicative of an autoimmune disease, administering to said patient at least one therapeutically active substance effective in the treatment of the autoimmune disease.

78. In combination, a kit as defined in any of claims 38 to 72, and at least one therapeutically active substance effective in the treatment of an autoimmune

disease.

79. A method substantially as hereinbefore described, substantially as described in one of the Examples.

80. A kit substantially as hereinbefore described, substantially as described in one of the Examples.

81. A kit substantially as hereinbefore described, substantially as illustrated in one or more of Figures 1a, 1b, 2a, 2b, 3a, 3b, 4, 5, 6, 7a, 7b, 8a, 8b, 8c, 8d, 9a, 9b, 10a or 10b.

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